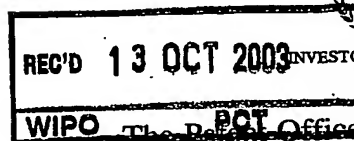


Rec'd PCT/PTO 08 DEC 2004

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The Patent Office

Cardiff Road
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1. Your reference

P31928-/NBW/BPU

2. Patent application number
(The Patent Office will fill in this part)

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0217930.7

3. Full name, address and postcode of the or of each applicant(underline all surnames)

Glycologic Limited
Glasgow Caledonian University
School of Biological and Biomedical Sciences
City Campus, Cowcaddens Road, Glasgow

08438202001

Patents ADP number(if you know it)

1198015

If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention

"A Chemical Carrier"

5. Name of your agent(if you have one)

Murgitroyd & Company

"Address for service" in the United Kingdom to which all correspondence should be sent (Including the postcode)

Scotland House
165-169 Scotland Street
Glasgow
G5 8PL

Patents ADP number(if you know it)

1198015

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and(if you know it) the or each application number

Country

Priority application number
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Date of filing
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Number of earlier application

Date of filing
(day / month / year)

8. Is a statement of inventorship and of right to grant of a patent required in support of this request?(Answer 'Yes' if:

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- a) any applicant named in part 3 is not an inventor, or
 - b) there is an inventor who is not named as an applicant, or
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Description 24

Claim(s)

Abstract

Drawing(s) 2 

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Priority documents

Translations of priority documents

Statement of inventorship and right to grant of a patent(Patents Form 7/77)

Request for preliminary examination and search(Patents Form 9/77)

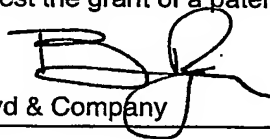
Request for substantive examination (Patents Form 10/77)

Any other documents (please specify)

11.

I/We request the grant of a patent on the basis of this application

Signature

Murgitroyd & Company 

Date

1 August 2002

12. Name and daytime telephone number of person to contact in the United Kingdom

PURDY, Hugh Barry

0141 307 8400

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1 A Chemical Carrier

2

3 The invention relates to solid and liquid
4 formulations comprising an active agent and a
5 carrier for the active agent.

6

7 Starches are comprised of α -glucans (amylose and
8 amylopectin in variable proportions, amounting to
9 ~82 to 89%), moisture (~11 to 17%), lipids (cereal
10 starches only, <1.5%) and protein (~0.5%) with some
11 α -glucan phosphate-esters (especially in potato
12 amylopectin). Plants produce starches in different
13 sizes and shapes which reflect the botanical origin.
14 In rice starch for example, the granules are <5 μ m in
15 diameter while in potato starch they may exceed
16 50 μ m. The amylose fraction of starches comprise
17 predominantly linear α -(1-4)-glucan molecules with a
18 molecular weight of ~0.25 million Daltons.
19 Amylopectin molecules are much larger with a
20 molecular weight of a few million Daltons and
21 comprise a heavily branched structure of small unit

1 chains (~15 to 80 glucose units long). The unit
2 chains are like amylose α -(1-4)-glucans (~95% of
3 bonds) but are linked together by α -(1-6) bonds
4 (~5%). Native starch granules contain double helices
5 of amylopectin which associate together to form
6 crystalline laminates which are interspersed with
7 amorphous amylopectin and amylose chains.

8
9 The properties of native starches from different
10 botanical origins may be modified by genetic,
11 chemical, enzymatic and/or physical processing.
12 During the last few centuries, novel mutations have
13 been developed where the ratio of amylose to
14 amylopectin in the starches has been modified to
15 create 'high amylose' starches where the α -glucan
16 fraction may represent >70% amylose (<30%
17 amylopectin) and 'waxy' starches where the
18 amylopectin fraction may represent >70% amylopectin
19 (<30% amylose). Modern methods of 'transgenic'
20 technology may also be used to create novel glucans
21 within starch granules with different chain lengths,
22 distributions and potentially even sugar residues
23 other than glucose. Chemical methods have been used
24 to enhance the properties of starch granules where
25 residues may be added by chemical bonding,
26 stabilisation may be achieved by cross-linking or
27 molecular weight may be reduced by hydrolysis (with
28 for example acids). Glucose syrups may be made from
29 starches by acid hydrolysis but are more often made
30 by enzymatic hydrolysis (below). Here, amylases
31 (specifically α -amylase) and amyloglucosidase can be
32 used to produce syrups with variable proportions of

1 different chain lengths and sugars (glucose and
2 maltose). Physically, starches may be pre-
3 gelatinised (heated in water to remove crystallinity
4 and dried to make 'instant' products) or damaged
5 (e.g. milled to remove ordered structure) to
6 moderate their functionality also.

7
8 Dextrins represent hydrolytic products of starches.
9 They are produced using a number of approaches as
10 discussed above.

11
12 Extensive acid hydrolysis may be used to produce low
13 molecular weight dextrins (<degree of
14 polymerisation, DP, ~20) where they may be branched
15 or linear, together with sugars in variable
16 proportions. The extent of hydrolysis is described
17 relative to the amount of reducing power compared to
18 a standard dextrose solution (dextrose equivalence,
19 DE). When glucose syrups are purchased they are
20 defined in terms of DE which suit specific
21 applications. These products are used extensively in
22 the food industry in confectionery, desserts,
23 drinks, cakes and pastries etc. where there is a
24 requirement for sweetness and product 'body'. In the
25 pharmaceutical industry there is a similar need for
26 glucose syrups in for examples pastilles and
27 tinctures with a need for pure glucose (dextrose) in
28 for example intra-venous products.

29 Less extensive acid hydrolysis of starches (with
30 some transglucosidation and repolymerisation) is
31 achieved by treating dry starches with acids and
32 heating at high temperatures. These dextrin products

1 are described as 'pyrodextrins' which readily
2 disintegrate in water and progressively solubilise.
3 They are classified as 'white', 'yellow' or 'British
4 Gums'. These dextrins have varying disintegrating
5 and solubilising characteristics and have specific
6 applications as for example tablet excipients.

7
8 Cyclodextrins are ring forms of dextrin oligomers.
9 The rings may contain six, seven or eight glucose
10 residues forming a hydrophobic core and hydrophilic
11 exterior. Hydrophobic residues (e.g. drugs) may be
12 located inside these cores and provide a vehicle for
13 drug delivery. A number of manufacturers prepare
14 cyclodextrins and their industrial utilisation is
15 quite well established (below).

16
17 Unlike the pyrodextrins, α -(limit)-dextrins
18 generated by α -amylase hydrolysis are not employed
19 as high molecular weight products (where there is
20 limited hydrolysis), either in the food or
21 pharmaceutical sectors. Similarly, β -limit dextrins
22 produced by hydrolysis of soluble starches
23 (generating the dextrins from amylopectin and
24 maltose sequentially from the α -glucan non-reducing
25 ends) are not used extensively in these industries.
26 The α -limit dextrins become more soluble as
27 hydrolysis is extended which, although random, is
28 initially restricted to starch amorphous regions.
29 The β -limit dextrins are highly soluble as exterior
30 chains of amylopectin have been hydrolysed (to
31 maltose) leaving short stubs attached to the (high

1 molecular weight) branched limit-dextrin residues.
2 β -limit dextrans are not at present commercially
3 available.

4
5 According to the National Starch web directory
6 (<http://www.foodstarch.com/directory>), a dextrin may
7 be defined as:

8
9 'Dextrans are starch hydrolysis products obtained in
10 a dry roasting process either using starch alone or
11 with trace levels of acid catalyst. The products are
12 characterised by good solubility in water to give
13 stable viscosities. Four types exist: White, Yellow,
14 British Gums and Solution-stable dextrans.'

15
16 Note that in reference to this commercially accepted
17 term, citations in patents referring to the use of
18 'dextrans' (e.g. Gregory (1983) and Gole et al
19 (1994), as discussed below) exclude β -limit dextrans
20 since they can only be produced in the solubilised
21 and not the dry state.

22
23 The properties of different dextrans are, as
24 discussed above, very different in terms of their
25 chemical and physical properties. They also have
26 different properties with respect to their potential
27 to be hydrolysed by different enzymes. Comparisons
28 are broadly made as follows:
29 Comparison of properties of different dextrans

- 1 Note that commercial 'dextrins are produced by heating
- 2 starches in the presence of a very small amount of acid
- 3 which induces hydrolysis, transglucosidation and
- 4 repolymerisation.

Dextrin	Product characteristics	Chemical properties	Physical properties
β -limit dextrin [Not a dextrin according to common commercial/ industrial usage of the term, see definition above]	White powder produced by hydrolysing solubilised amylopectin (from starch) with β -amylase	Molecular weight of dextrin ~ 50% that of amylopectin. Incorporates no amylose residues. Maltose would be present (from amylose and amylopectin hydrolysis) unless removed by for example dialysis or chromatography.	Soluble powder with no granular or crystalline form - i.e. amorphous.
British Gums [True commercial dextrin]	Dextrin, usually yellow or brown and darker than standard 'yellow dextrins' below. Powder form produced by roasting ~ dry starch at high temperatures at ~ neutral pH.	Hydrolysed starches incorporating residues of amylose and amylopectin which will incorporate some transglucosidation and repolymerisation	Dark coloured and relatively soluble - especially when heated - in water.
Maltodextrin [Not a dextrin]	Produced from extensive acid or	Branched dextrins comprising	Soluble dextrins with reducing power

according to common commercial/ industrial usage of the term, see definition above]	α -amylase (α -limit dextrin) hydrolysis of starch. Component of glucose syrups.	α -(1-4) and α -(1-6) bonds. Low molecular weight (degree of polymerisation, DP, $< \sim 20$) soluble branched product.	much greater than starch polysaccharides but less than free sugars. Dextrose equivalence (DE), 5-20.
White Gums [True commercial dextrin]	Dextrin, usually ~ white. Powder form produced by roasting ~ dry starch at relatively low temperatures at low pH.	Hydrolysed starches incorporating residues of amylose and amylopectin which will incorporate some transglucosidation and repolymerisation	Light coloured and relatively soluble - especially when heated - in water.
Yellow Gums (also referred to as Canary Gums) [True commercial dextrin]	Dextrin, yellow. Powder form produced by roasting ~ dry starch at relatively high temperatures at low pH.	Highly converted hydrolysed starches incorporating residues of amylose and amylopectin which will incorporate some transglucosidation and repolymerisation	Yellow coloured and relatively soluble - especially when heated - in water.

- 1 Cyclodextrins and their derivatives have been used
- 2 extensively in pharmaceutical applications and details
- 3 may be found in a number of patent sources (e.g. Uekama
- 4 et al, 1989).

1 One important application of solid dose formulations is
2 the application in rapid release oral dose (buccal
3 melt) type formulations. These products have been
4 described by Ohno et al (1999) in relation to their
5 buccal type formulations and those of their
6 competitors. The proposed advantage of the Ohno et al
7 (1999) technology over their competitors is the
8 capacity to make solid formulations that might
9 disintegrate rapidly. The technology describes the use
10 of a pharmaceutically active agent, erythritol,
11 crystalline cellulose and a disintegrant.

12

13 Fast dissolving formulations have been described by
14 Makino et al (1993) where they describe the use of an
15 active ingredient, a carbohydrate and a barely
16 sufficient amount of water to moisten the surface of
17 particles of the said carbohydrate into a tablet form
18 and a fast dissolving tablet obtained by this method.
19 The carbohydrate fraction is defined as to include
20 sugar, starch-sugars, lactose, honey, sugar alcohols
21 and tetroses with tablets which are porous with
22 excellent digestibility, solubility and adequate
23 strength. It is stated that the carbohydrate to be
24 employed must be 'soluble in water and does not
25 adversely affect the active ingredient (for example,
26 decomposition of the active ingredient)'. The
27 disclosure concentrates on sugars as they would be
28 expected to dissolve and disperse apart from the active
29 ingredients in tablets without entrapment-type
30 interactions upon hydration. The disclosed preference
31 is to use 'sucrose, glucose, maltitol, xylitol,
32 erythritol and so on' [sugar and sugar alcohols but no

1 mention of oligo- or polysaccharides]. Also mentioned
2 are 'sugar, starch-sugars, lactose, honey, sugar-
3 alcohols, tetroses, sucrose, coupling-sugars,
4 fructooligosaccharides, palatinose and so on'. Sugars
5 are elaborated as 'glucose, maltose, powdered syrup,
6 starch syrup, isomerised sugar (fructose) and so on'.
7 For lactose they elaborate as 'lactose, isomerised
8 lactose (lactulose), reduced lactose (lactitol)'. For
9 sugar alcohols they include sorbitol, mannitol, reduced
10 malt syrup (maltitol), reduced starch saccharides,
11 xylitol, reduced palatinose and so on'. Tetroses are
12 defined as obtained from glucose fermentation.

13
14 Zydis is a technology platform owned by R P Scherer
15 where fast dissolving formulations are manufactured by
16 blending and dissolving an active ingredient with a
17 polymer, sugar and other ingredients followed by freeze
18 drying (lyophilisation or in the context of the patent
19 description 'sublimation'). Although some authors have
20 proposed that freeze dried formulations are problematic
21 and have proposed solvent extractable matrices or
22 matrices incorporating solvent sublimation to add
23 advantage (Gregory et al, 1983; Gole et al, 1994) the
24 Zydis technology is still popular. Gregory et al (1983)
25 and Gole et al (1994) discuss the use of dextrans in
26 their (sublimed/freeze dried) delivery matrices but do
27 not define which type of dextrin which is very
28 confusing in view of the very different chemistries and
29 physical properties of different dextrans. The authors
30 do not have interests in tablet production (by
31 compression) per se. In reality, only some dextrans
32 would impart desirable characteristics (forming the

1 appropriate structure and melt type characteristics) in
2 these freeze dried matrix types whilst others would be
3 detrimental. For example, the dextrans present in
4 maltose syrups have a very low molecular weight and
5 would be very different (size, shape, structure,
6 solubility, reducing power, rheology, digestibility
7 etc.) from dextrans produced from very limited (acid or
8 α -amylase) hydrolysis of native starches. In fact, the
9 only example Gregory (1983) cite is 'dextrin' (not
10 type, source etc.) while the Gole et al (1994)
11 application is based on (exemplified by) maltodextrin
12 (which is generated by α -amylase but not β -amylase as
13 previously discussed). It is apparent in these patents
14 that the applicants do not understand the breadth of
15 different chemical species and properties in different
16 types of dextrans. Different dextrans have different
17 properties and chemistries.

18

19 According to the invention, there is provided a solid
20 unit dose product comprising an active agent and a
21 carrier for the active agent, wherein the carrier
22 comprises β -limit dextrin.

23

24 In a preferred embodiment of the invention, the unit
25 dose product is a pharmaceutical product such as, for
26 example, a fast melt or slow melt tablet, a freeze
27 dried matrix, a wafer, a pellet or the like. Suitably,
28 therefore, the unit dose product may be a capule
29 comprising a pharmaceutical formulation enclosed within
30 a hard or soft shell. In such cases, either or both of
31 the shell and the enclosed formulation may include β -
32 limit dextrin.

1 In this specification, the terms "pharmaceutical
2 product" and "pharmaceutical preparation" should be
3 understood to include therapeutic and prophylactic
4 pharmaceutical products as well as health promoting
5 agents such as vitamins, minerals, herbal remedies,
6 proteins, amino acids and the like.

7

8 The invention also relates to a particulate product
9 comprising an active agent and a carrier for the active
10 agent, wherein the carrier comprises β -limit dextrin.
11 In this specification, the term "particulate product"
12 should be understood to include powders, granules and
13 flakes. Typically, the particulate product is derived
14 from pulverised freeze dried matrices or spray dried
15 material. Suitably the particulate product is a
16 pharmaceutical product. In one embodiment of the
17 invention, the particulate product is an inhalation-
18 type product. The invention also relates to a liquid
19 formulation comprising an active agent and a dispersing
20 agent for the active agent, wherein the dispersing
21 agent is β -limit dextrin. Typically, the liquid
22 formulation is a pharmaceutical formulation such as,
23 for example, a tincture, however, non-pharmaceutical
24 liquid formulation are also envisaged.

25

26 The invention also relates to the use of β -limit
27 dextrin as an excipient in pharmaceutical formulations,
28 either as a sole excipient or as one of a plurality of
29 excipients. The invention also relates to the use of β -
30 limit dextrin as a dispersant in liquid pharmaceutical
31 and non pharmaceutical formulations. The invention

1 also relates to the use of β -limit dextrin as an
2 excipient in fast-melt solid unit dose pharmaceutical
3 products.

4

5 The invention also relates to the use of β -limit
6 dextrin as a disintegrant in solid products such as
7 pharmaceutical and detergent formulations and the like.

8 The invention also relates to liquid formulations
9 reconstituted from a solid formulation of the
10 invention.

11

12 Melt Formulations

13

14 These are rapidly disintegrating formulations which are
15 intended to be dissolved very rapidly in the buccal
16 cavity (mouth). Generally these formulations lack
17 physical strength.

18

19

20 Use of β -limit dextrans in freeze dried matrices and 21 tablet (including melt) type formulations

22

23 These have not been defined elsewhere. As discussed
24 above, freeze dried matrices have been described
25 (containing 'dextrans') but do not incorporate the use
26 of β -limit dextrans. Furthermore, tablet formulations
27 with melt or slow release type formulations have not
28 been described at all where β -limit dextrans have been
29 incorporated. The unique characteristics of β -limit
30 dextrans in freeze dried matrices and tablets are

1 unexpected and surprisingly as presented later in this
2 application.

3

4 Powder formulations incorporating β -limit dextrins

5

6 These molecules can be formed from dried matrices (e.g.
7 from pulverised freeze dried matrices or from spray
8 dried material). We have found that active agents can
9 be incorporated into these matrices before drying or
10 blended together subsequently. These applications are
11 discussed below. This material clearly has applications
12 in tablets (above), sachets etc. and as an inhalation
13 type (pulmonary) carrier as the material is quite
14 'sticky' when hydrated.

15

16 Liquid formulations incorporating β -limit dextrins

17

18 This dextrin is highly soluble. Also, because of the
19 removal of exterior chains (of amylopectin) the product
20 cannot retrograde (recrystallise) easily if at all from
21 solution. This makes the product very stable in
22 solution and appropriate as a dispersing component in
23 liquid pharmaceutical (and non-pharmaceutical)
24 preparations.

25

26 The invention will be more clearly understood from the
27 following description of some embodiment thereof, given
28 by way of example only, with reference to the
29 accompanying Figures in which:

30

31 Figure 1 is a graph illustrating the rheological
32 properties of a product according to the invention; and

1 Figures 2 and 3 illustrate the dissolution properties
2 of a number of products according to the invention
3

4 β -limit Dextrin Production
5

6 These dextrans may be produced from starches of
7 different botanical origins and different genetic
8 modifications, chemical, enzymatic or physical
9 derivatives. Since all the amylose is converted to
10 maltose, it is much more cost effective to use high
11 amylopectin ('waxy type') starches where there is a
12 higher proportion of amylopectin - the origin of the β -
13 limit dextrin.
14

15 The dextrin may be produced by a number of routes and
16 the following method does not exclude material produced
17 by other routes nor using other sources of enzyme or
18 processing conditions.
19

20 The dextrin is produced in conjunction with maltose
21 from the α -glucan hydrolysis. In the method described
22 below, the maltose is removed by dialysis leaving pure
23 dextrin. However, the maltose could be left in the
24 product as an option (to impart sweetness and novel
25 functionality).
26

27 Waxy maize starches (c. 25g) were dissolved in 500ml
28 acetate buffer (0.02M, pH 4.8) at 100°C for at least 1
29 hour. After cooling to room temperature, crystalline
30 sweet potato β -amylase (5×10^3 units, Sigma A-7005) was
31 added and the mixture was thoroughly mixed. The mixture

1 were then transferred into dialysis tubing (Visking
2 code DTV 12000.13.000) and incubated for 36 hours at
3 37°C under dialysis against the same buffer, which was
4 renewed three time during the first 3 hours and twice
5 afterwards. After the reaction had been terminated by
6 heating the mixture for 10 mins at 100°C, the
7 coagulated protein was removed by centrifugation, and
8 then ethanol were added to the solution. The resulting
9 precipitate was collected by centrifugation, dissolved
10 in water (250ml) and then re-precipitated by the
11 addition of ethanol. The precipitate recovered on
12 centrifugation was finally dissolved in water and then
13 dried (below).

14

15 Drying Tests

16

17 Dextrin alone

18

19 The dextrin was dried using freeze drying and spray
20 drying (including use of small pilot scale Büchi mini
21 spray dryer model B-191). The spray dried material is a
22 fine powder with good flow characteristics. The freeze
23 dried material makes a fine lyophilised matrix. This
24 may be milled to a powder which tends to be a little
25 electrostatic in character.

26

27 Dextrin Characterisation

28

29 The product of β -amylase hydrolysis was analysed by gel
30 permeation chromatography (GPC, using Sepharose CL-2B
31 gels) according to Karkalas and Tester (1992) before
32 and after dialysis (to remove maltose). Accordingly the

1 retention time and molecular weight of the dextrin was
2 smaller than the native amylopectin (with maltose
3 present prior to dialysis). This confirms that the
4 native amylopectin molecules were selectively
5 hydrolysed.

6

7 Rheological Properties

8

9 To prove that the rheological properties of a drug in
10 solution with a sugar (glucose) or the β -limit dextrin
11 are different in terms of interactions the following
12 experiment was conducted.

13

14 Samples of theophylline and either glucose or the β -
15 limit dextrin were dispersed in water (to give a
16 concentration of 1% theophylline, w/w and either 1%
17 with respect to glucose or beta-limit dextrin, w/w)
18 within sealed screw capped tubes. These were sealed and
19 mixed and kept in a 25°C water bath. The viscosity was
20 immediately determined using a Brookfield DV-III
21 Viscometer (Brookfield Engineering Laboratories, INC.,
22 USA) fitted with a cone and spindle CP-40 system (2.4cm
23 dimension and 0.8° angle) with a thermostatically
24 controlled temperature of 25°C. A silicon viscosity
25 standard (96.2mPas at 25°C) from Brookfield was used
26 for calibration.

27

28 Enzyme digest with or without dialysis to remove
29 maltose.

1 The properties of formulations containing the dextrin
2 which have none, some or all of the maltose remove
3 (howsoever) differ in their properties. These are
4 considered below.

5

6 Applications

7

8 **Examples**

9

10 1. Tablet Formulations

11

12 It was found that the dextrin could be tableted
13 directly to form products with different drugs. The
14 following examples exemplify this.

15

16 a. Direct compression

17

18 β -limit dextrin was prepared from waxy maize starch and
19 was spray dried to form a fine powder.

20

21 b. Granulation

22

23 Samples (15g) of the β -limit dextrin (dried by freeze
24 drying) was wet massed with 5ml water using an FP296
25 mixer (Kenwood Ltd, UK). Granules were then spread
26 evenly over a drying tray and dried overnight at 60°C.
27 Dried granules were passed through a 300 μ m mesh to
28 produce a free-flowing powder.

29

30 Two formulations were produced using the same water-
31 soluble drug but different types of additional
32 tableting excipient since the tablet release matrix

1 (first) formulation was not easily tabletable with drug
2 alone (as friable tablets were produced). Each
3 formulation was then tested using a standard USP II
4 paddle dissolution apparatus (ST-7 model, Caleva Ltd,
5 UK) at 37°C in 1000ml water (λ_{\max} propranolol.HCl =
6 298nm).

7

8 Formulation 1. β -limit dextrin, hydrophilic excipient
9 and tablet release formulation

10

11 Formulation:

12 40% β -limit dextrin

13 20% Microcrystalline cellulose (Avicel 101)

14 20% Lactose

15 20% Propranolol.HCl

16

17 The formulation was mixed for 30 minutes using an
18 orbital Turbula™ mixer (Glen-Creston Ltd, Middlesex,
19 UK). The resultant mixture was then tabletted with a
20 7.95mm concave punch and die set using an E2 single
21 punch tablet press (BWI-Manesty Ltd, Liverpool, UK).

22

23 Tablet properties made according to hydrophilic tablet
24 Formulation

No.	Weight (mg)	Thickness (mm)	Hardness (N)	Diameter (mm)
1	194.9	3.99	36	7.95
2	201.6	4.09	40	7.94
3	181.6	3.79	28	7.93
4	201.0	4.06	46	7.93
5	179.6	3.75	25	7.93
6	190.7	3.95	32	7.96
7	177.9	3.73	32	7.94
8	194.3	4.00	24	7.94
Mean	190.2	3.92	33	7.94
SD	± 9.4	± 0.14	± 7	0.01

1 Formulation 2. β -limit dextrin, hydrophobic excipient
 2 and tablet release formulation

3

4 Formulation:

5 50% β -limit dextrin

6 25% Emcompress® (Dibasic calcium phosphate)

7 25% Propranolol·HCl

8

9 The components were mixed and compressed as with the
 10 previous formulation (1).

11

12 Tablet properties made according to hydrophobic tablet
 13 formulation

No.	Weight (mg)	Thickness (mm)	Hardness (N)	Diameter (mm)
1	205.0	3.91	<10	7.94
2	192.9	3.72	<10	7.94
3	197.4	3.85	<10	7.94
4	199.2	3.78	<10	7.94
5	199.9	3.76	<10	7.96
6	194.0	3.74	<10	7.94
7	193.7	3.65	<10	7.96
8	197.4	3.83	<10	7.97
Mean	197.4	3.78	<10	7.94
SD	± 4.0	± 0.08		0.01

1 Better weight uniformity is obtained indicative of
 2 improved powder flow. Low hardness may be improved by
 3 adding a compression binding agent.

4

5 2. Dried matrices

6

7 Solutions/suspensions containing the dextrin and
 8 theophylline (e.g. 10% with respect to the dextrin and
 9 0.1% with respect to theophylline) were freeze-dried
 10 where easily hydratable matrices were formed. These
 11 melt type formulations can also be milled to produce
 12 fine powders.

13

14 The matrices 'melted' or rather dissolved and dispersed
 15 exceedingly easily when water came into contact with
 16 them. It is evident that freeze-dried products could be
 17 made from this material.

1 3. Powder Formulations

2

3 These may be made from milling dried matrices (e.g.
4 '2'). However, powders can also be made directly by for
5 example spray drying.

6

7 Solutions containing the dextrin and theophylline (e.g.
8 10% with respect to the dextrin and 0.1% with respect
9 to theophylline) were spray dried where very fine
10 powders were prepared that disperse very easily upon
11 hydration. These may be tableted (see above) or
12 utilised in sachet type formulations. It is anticipated
13 that pulmonary type delivery products could be made
14 from small particles comparable or smaller than
15 dimensions present in these powders.

16

17 4. Liquid Formulations

18

19 The β -limit dextrin was dissolved in water (for example
20 a 10% solution) with theophylline (for example 0.1%).
21 The solution was found to be very stable at room
22 temperature and could be used as a liquid formulation
23 for oral delivery of drugs and for parenteral
24 administration.

25

26 5. Enhancement of drug solubility

27

28 It was noted that rather surprisingly the β -limit
29 dextrin could facilitate the dissolution of drugs.
30 There are many potential applications with respect to
31 dispersing and solubilising insoluble compounds. The
32 following example indicates that this is so.

1 6. Dialysis

2

3 It is also apparent that the material could be
4 potentially used for intra-peritoneal dialysis if a low
5 osmotic α -glucan is required. The product would
6 potentially fulfil the need in this area provided by
7 oligosaccharide type products like 'icodextrin'
8 produced by ML Laboratories. The following example
9 indicates that this is so.

10

11 7. Adhesions

12

13 Similarly to the icodextrin product discussed above, it
14 is anticipated that the material could function to
15 prevent tissue adhesion. This is because as follows.

16

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18

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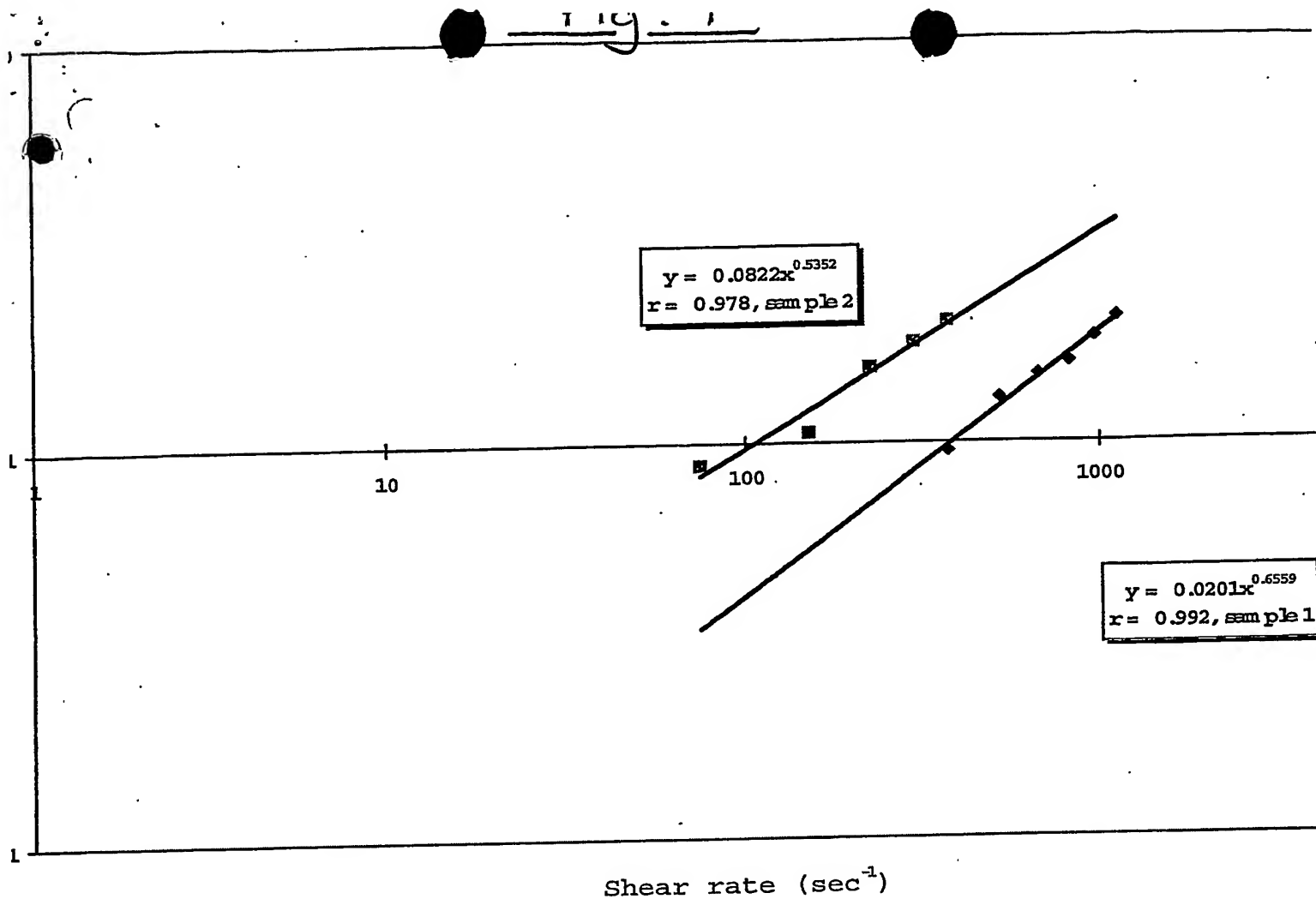
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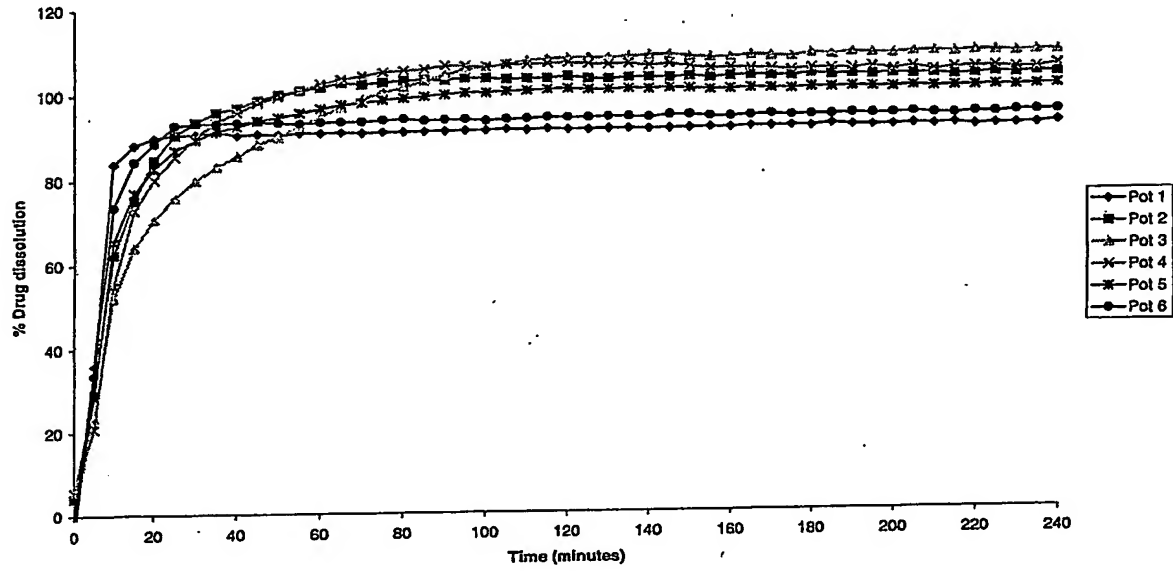


Sample 1: glucose solution contains 1% glucose and 1% theophylline
 Sample 2: beta-limit dextrin solution contains 1% beta-limit dextrin and 1% theophylline).

Fig. 2

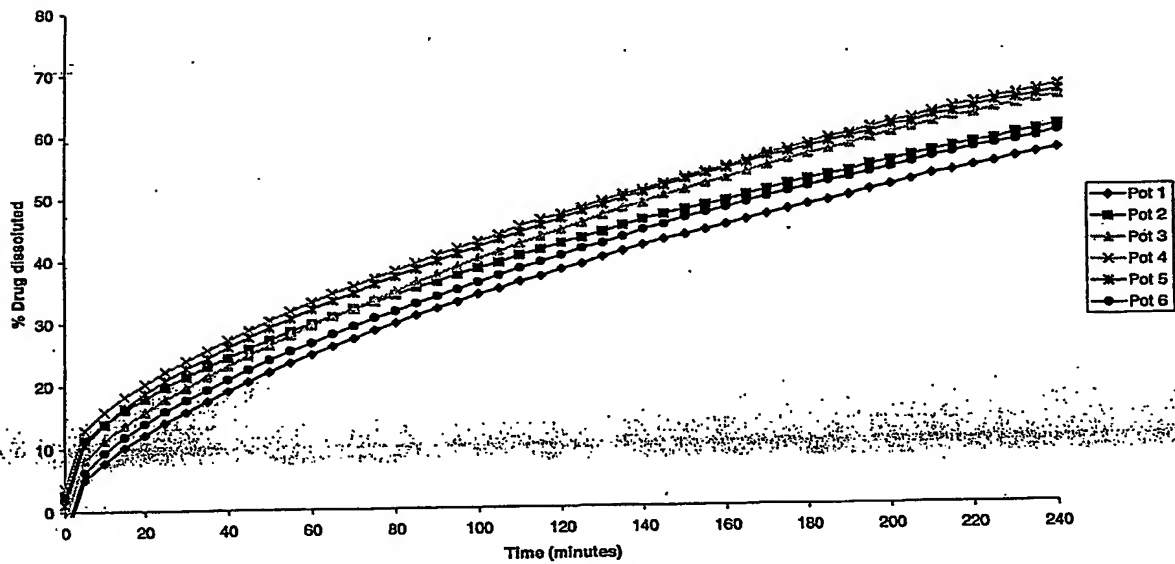
Dissolution Data

Formulation 1.



Formulation 2.

Fig. 3



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